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TITLE: A Population-Based Study of Dietary Acrylamide and Prostate Cancer Risk

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14. ABSTRACT <u>Purpose/scope:</u> The aim of this study is to determine whether intake of foods found to have high levels of acrylamide increase the risk of prostate cancer among men. <u>Major findings:</u> We have finished the data collection in a population-based case-control study on prostate cancer. The daily median intake of acrylamide was 43 microgram in the control group. <u>Up-to-date report:</u> The project is up and running, but due to problems with the laboratory method for analysis of DNA adducts of acrylamide and the delayed payment from US army, we have been granted one additional year in order to finish the tasks for months 13-29 (see "Research accomplishments"). We foresee no problems in completing them on schedule.					
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1. Introduction

The substance acrylamide is a chemical that impairs the nervous system and has been classified as a probable carcinogen by the International Agency on Cancer Research (IARC 1995). Recently, the Swedish National Food Administration found high levels of acrylamide in a variety of foodstuffs, including French fries, potato crisps, and crispy bread. It is thought that acrylamide formation occurs during the heating of starch-rich foods to high temperatures. Because the foodstuffs containing acrylamide are commonly consumed both in the US and Sweden, this report created substantial international alarm about the public's health. Several studies on animals exposed to toxic levels of this chemical, which found that acrylamide increases the risk of a variety of cancers in a dose-response relationship. There is, however, scant human data on the carcinogenic effect of acrylamide. The studies on humans thus far have been limited to acrylamide contact in the occupational setting. This project will examine the hypothesis that high intake of foods containing acrylamide increases the risk of prostate cancer among men. We will address the study questions using information from a case-control study of prostate in Sweden. Research in Sweden has a number of advantages, including the use of nationwide cancer registry and the use of national registration numbers uniquely identifying all Swedish residents, which offer opportunities for population-based, cost-effective and reliable studies. The incidence of prostate cancer in Sweden is similar to rates seen in the United States. In addition, both countries have similar consumption of the foods with high levels of acrylamide.

2. Body

Research accomplishments as outlined in the Statement of Work.

Task 1. Data collection, Months 1-6:

- a. End the data collection of questionnaire and blood sample,
- b. Transfer questionnaire data into electronic format

Summary: We have successfully finished the data collection of a population-based case-control study on prostate cancer in Swedish men. We have questionnaire data (including a food frequency questionnaire) from 1,499 cases and blood from 1,400 cases. We have questionnaire data from 1,130 controls and blood from 879 controls. The questionnaire data have been transferred to an electronic format.

Task 2. Database management of data file, Months 7-12:

- a. A database quality control program will be instituted to check for data errors and inconsistencies in the questionnaire database from the population-based case-control study.
- b. The food frequency questionnaire will be translated into a nutrient database.
- c. Data on acrylamide levels in specific food products will be accessed from the Swedish Food Administration.
- d. An algorithm will be developed to estimate acrylamide indices for specific food products.
- e. An overall estimate of dietary acrylamide exposure will be developed for each study participant.

- f. Additional statistical programming will be undertaken to translate and create new variables.
- g. A final data quality control protocol will be instituted to minimize errors in the database.
- h. A final file including questionnaire data, food and nutrient data, and the record linkage will be output into a SAS dataset.

Summary: An extensive effort has been made to clean the data set of errors and we are now confident that it can be used for analysis. All the sub-tasks described above (a-h) have been accomplished.

Task 3. Analysis of Hb adducts from acrylamide in blood. Months 13-18:

- a. Preparation of blood samples from the biobank.
- b. Isolation of hemoglobin.
- c. Detachment of adducts from the hemoglobin.
- d. Isolation of the detached adduct.
- e. Derivation of the adducts.
- f. Analysis of the adducts.

Summary: This work is ongoing. We have successfully received 400 blood samples from the Biobank and the isolation of hemoglobin has been done on all of them. Analyses of DNA adducts have been performed on the 100 samples so far.

Task 4. Data Analyses, Months 19-24:

- a. The data analysis plan will be detailed and analysis of the final data set will be conducted.

Summary: This work is ongoing.

Task 5. Report and Manuscript Production, Months 25-29:

- a. Manuscripts will be prepared.
- b. A final report of the findings will be written.

Summary: These tasks have not yet been initiated.

3. Key research accomplishments

1. The data collection from a large population-based case-control study on prostate cancer has been completed. 42% of the cases were classified as advanced cases. Both questionnaire data on food habits and blood samples were collected.
2. The daily median intake of acrylamide in the control group was 43 microgram. The range was 0-159 microgram/day.
3. The four food products that contributed the most to the total intake of acrylamide among controls were crisp bread, coffee, fried potato, and whole grain bread (73% of the total intake).

4. Reportable outcomes

At this stage, there are no reportable outcomes.

5. Conclusions

As outlined under "Research accomplishments", we have finished tasks 1 and 2, and are well on the way with task 3. It has taken us somewhat longer than anticipated to get the laboratory analyses of DNA adducts up and running due to technical problems with a new and improved method. In addition, due to the delayed payments from the US army, we have not had the resources to work at the speed that we planned at the start of this project.

We found that the intake of acrylamide from diet in this male population is in line with recent reports by us about the intake of acrylamide in the Swedish populations (Mucci 2003; 2005). The level of exposure is much lower than was anticipated by the National Food Administration when the presence of acrylamide in food products was first discovered in the year of 2002.

6. References

1. IARC Monographs on the evaluation of carcinogen risk to humans: some industrial chemicals, No. 60, International Agency for Research on Cancer, Lyon, 1994.
2. Mucci L, Dickman P, Steineck G, Adam HOi, Augustsson K. Dietary acrylamide and risk of cancer of the large bowel, kidney and bladder: Absence of an association in a population-based study in Sweden. *British Journal of Cancer* 2003;88:84-89.
3. Mucci L, Sandin S, Bälter K, Magnusson C, Weiderpass E, Adami HA. Acrylamide intake and breast cancer risk in a large, prospective study among Swedish women. *JAMA* 2005 Mar 16;293(11):1326-7.

7. Appendices

None.